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MOSQUITOES, MALARIA AND THE WAR IN THE PACIFIC[1]

By EDWARD PHILPOT MUMFORD

OXFORD UNIVERSITY AND STANFORD UNIVERSITY

THE recent fall of Bataan was attributed mainly to malaria and lack of quinine by the United Press correspondent, Frank Hewlett, writing in *The New York Times* for April 18, and other observers. In the last war malaria took first place among the diseases responsible for casualties. Even in normal times, it is one of our most important public health problems. With the Dutch East Indies now largely in enemy hands, the principal source of supply of the world's quinine is lost to the United Nations, and although synthetic anti-malarials have been in use for some time, one can not overestimate the seriousness of a quinine shortage. Because of a low toxicity, and the fact that careful medical supervision is not required, quinine is still the most valuable drug for malarial prophylaxis and the treatment of acute malaria. There is no drug known to-day which can completely replace quinine and the other cinchona alkaloids. Because of these and other factors which are obvious, it is particularly important at this time to consider

[1] "Studies on Faunal Distribution," No. 7. These studies have received the support of the Carnegie Corporation of New York, the National Academy of Sciences, the American Association for the Advancement of Science, the Society of Sigma Xi, the American Philosophical Society, the May Esther Bedford Fund, Incorporated, and various subscribers to the Oxford University Chest. See G. D. Hale Carpenter, SCIENCE, 95: 325–326, 1942.

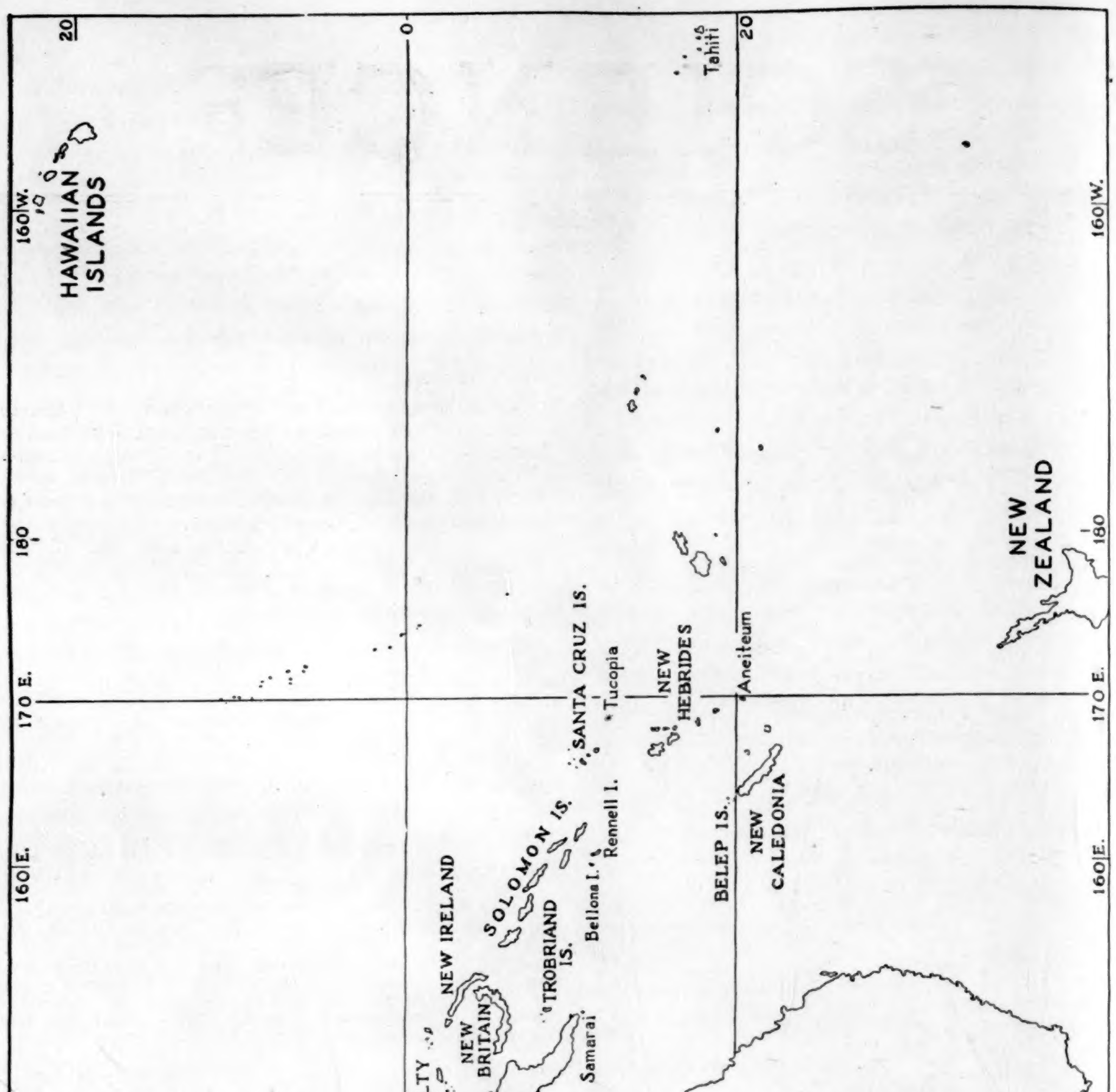
HAWAIIAN ISLANDS
PHILIPPINE ISLANDS
Bataan Pen.
JAVA
NEW GUINEA
ADMIRALTY IS.
NEW BRITAIN
NEW IRELAND
TROBRIAND IS.
Samarai
SOLOMON IS.
Bellona I.
Rennell I.
SANTA CRUZ IS.
Tucopia
NEW HEBRIDES
Aneiteum
BELEP IS.
NEW CALEDONIA
Tahiti
NEW ZEALAND
A U S T R A L I A
MERCATOR PROJECTION
120 E.
140 E.
160 E.
170 E.
180
160 W.
20
0
20

FIG. 1.

the distribution of malaria and its carriers, the *Anopheles* mosquitoes, in the Pacific theater of the war.

According to P. A. Buxton, malaria is "believed to occur in all the islands between the equator and 20° S., from New Guinea eastwards to 170° E. The only islands inside this area which are free from malaria are Belep, to the northwest of New Caledonia, and a very few minute islands such as Tucopia. The only malarious island outside that area is Aneityum, which is a fraction of a degree further south than 20° S."[2] In his health surveys of 1930 and 1933, S. M. Lambert failed to find malaria in Rennell and Bellona Islands, but it has since reached Rennell (Lambert, *in lit.*, June 5, 1942), so Buxton's statement is now no doubt substantially correct. Authorities, however, do not agree as to the presence or absence of malaria and *Anopheles* in New Caledonia. M. A. Laveran, in *Comptes Rendus de la Société de Biologie* for 1901 and 1902, A. Leboeuf, in the *Bulletin de la Société de Pathologie Exotique* for 1913, and E. C. Zimmerman, in the *American Naturalist* for May–June, 1942, all specifically comment on the absence of *Anopheles* from New Caledonia. F. W. Edwards, in the "Genera Insectorum," 1932, and F. H. Taylor, in his "Check List of the Culicidae of the Australian Region," 1934, however, both include New Caledonia within the range of *A. punctulatus*. P. A. Buxton, in his review of Taylor's work in the *Tropical Diseases Bulletin* for 1935, does not accept this, and quotes Taylor as subsequently agreeing with him. Fritz Weyer, in "Die Malaria-Übertrager," 1939, however, again records *Anopheles* from New Caledonia. The question is of more than academic interest, as New Caledonia is a vitally strategic island along the supply route between the United States and Australia, and the United States has recently landed troops there.[3] If *Anopheles* are present there, the danger of infection is imminent and the troops will require daily prophylactic doses of such anti-malarials as are available; if they do not exist there, administration of drugs for malaria prophylaxis would be wasteful. In any case, a supply of quinine or a suitable synthetic substitute should be on hand, as *Anopheles* and malaria may be brought in from elsewhere.

The standard works of Edwards and of Taylor, mentioned above, to which the medical entomologist would naturally refer, are misleading in that they fail to give complete lists of the Pacific islands where *Anopheles* are definitely known to occur. Both Edwards and Taylor omit from the range of *Anopheles* the Admiralty and Trobriand Islands, New Britain, New Ireland, the Santa Cruz Islands and Samarai in the China Strait near New Guinea. Weyer omits the Admiralty, Trobriand and Santa Cruz Islands and Samarai. Kumm's paper in the *American Journal of Hygiene Monographic Series,* 1929, is more complete, but his record, now unacceptable, of a third species, the Australian *A. annulipes,* from the New Hebrides, was obtained by reducing *A. farauti* to a synonym of *A. annulipes* instead of *A. punctulatus,* as is now customary. Herms and Gray's record of *A. annulipes* from the New Hebrides, in "Mosquito Control," 1940, is no doubt derived from the same source.

As far as can be ascertained, there are at present in the Pacific Islands east of New Guinea two species and one variety of *Anopheles.* One of the species, *Anopheles punctulatus,* and its variety *molluccensis,* range into the Pacific as far east as the New Hebrides. Both are proven carriers of malaria. The other species, apparently as yet unnamed, is known only from the larvae taken in New Britain.

In view of the fact that an introduced *Anopheles,* carried from Africa by airplane or fast navy destroyer, was responsible for the wide-spread and devastating malaria outbreak in Brazil in 1931, it is important to consider the imminent danger of the spread of other members of the genus in the Pacific region. *Anopheles punctulatus* and its variety *molluccensis* have the most adaptable larvae of all known *Anopheles,* so they may be expected to extend their range beyond the New Hebrides and become established in new localities. According to Swellengrebel and Swellengrebel in the *Bulletin of Entomological Research* for 1920–21, *molluccensis,* wherever it occurs, is very common, breeding everywhere, in all kinds of water, fresh or salt, stagnant or running, dirty or clean. Larvae have been found even in water standing in coconut shells and in native boats. As early as 1928, fear of the introduction of *A. punctulatus* into Tahiti from the New Hebrides was expressed, and the danger of the spread of *Anopheles* through the Pacific islands is, of course, now increased immeasurably as a result of constantly increasing air traffic and disturbed conditions generally.

The islands of Mauritius, Reunion and Barbados long enjoyed immunity from *Anopheles* and malaria, but within the last century all three have suffered severe epidemics. It is not unlikely that New Caledonia, and even Hawaii and the islands of the Central Pacific, will lose their immunity before the end of the present war. As Herms and Gray write, the transport of a fertilized *Anopheles* to the Hawaiian Islands, where malaria is at present almost unknown, might

[2] *Trans. Roy. Soc. Trop. Med and Hyg.*, 19: 420–454, 1925–26. See also P. A. Buxton and G. H. E. Hopkins, "Researches in Polynesia and Melanesia," 3: 51–124, 1927.

[3] The recent outbreak of plague in New Caledonia is referred to elsewhere (E. P. Mumford, "Native Rats and the Plague in the Pacific," *American Scientist*, 30: 212–217, 1942).

ultimately become both a public health and an economic disaster to the Islands. With only a limited supply of quinine or other anti-malarials, the further spread of *Anopheles* and malaria might well affect an entire campaign and even the final outcome of the war in the Pacific.

The problem of mosquito control, which is of the utmost importance, is, of course, beyond the scope of this series of studies on faunal distribution. It has, moreover, been dealt with at length by leading authorities such as Herms and Gray.

As part of this series, revised lists of mosquitoes and other vectors of disease in the Pacific and other islands are being completed for publication in the hope that the dissemination of such information may be of use in the present emergency.

MECHANISM OF ACTION OF ORDINARY WAR GASES

By Professor CHAUNCEY D. LEAKE and DAVID F. MARSH

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CURRENT interest in war gases justifies pharmacological discussion of their mechanism of action. This may help to give a rational background for advice to civilians for reasonably effective protection against, and management of, possible war gas injury.

In general, the intensity of biological action of any chemical is determined by (1) the dosage, in terms of mass of chemical per mass of living material; (2) the ratio of the rate of absorption and distribution of the drug through the living tissue to its rate of excretion or destruction; (3) the physico-chemical properties of the drug, such as its differential solubility in different solvents, its polarity, its molecular configuration and energy organization, its dissociation characteristics and its optical properties, and (4) the peculiarities of the particular type of living tissue involved, such as its age, its metabolic and allergic states and its enzyme balance. These factors may be summarized in short-hand fashion in the following non-mathematical formula:

$$I = (f) \left[D \frac{rA}{rE} \right], \text{ Ch, P.}$$

The concentration (C) of the chemical in the tissues at any given moment after administration is given by the product of D and the ratio of rA to rE.

Consistent appreciation of these factors may aid both in understanding the difference in action of various war gases and also the variation in intensity of effect of the same war gas in the same concentration on different individuals. An appropriate analogy to the latter situation is the difference in response of different people to the same intensity of sunlight or poison ivy.

For this discussion we may limit ourselves to a consideration of the ordinary war gases, such as the lung irritants, like phosgene or chloropicrin, or the vesicants, like mustard gas and lewisite. We may thus disregard such unusual possibilities as catalyzed cyanides or metallic carbonyls, and such gaseous associates of demolition bombs and incendiaries as carbonmonoxide, "nitrous fumes," "blast," hot oil smoke or phosphorus. However, the tissue aggressiveness of "nitrous fumes" suggests that these deserve attention in the same way as ordinary war gases.[1]

As indicated in Table 1, the ordinary war gases may be considered to be chemical relatives of such types of aliphatic hypnotic and inhalation anesthetic agents as alcohol, chloroform and ether. There is general knowledge of the locally irritating powers of these common compounds. Their war gas relatives may owe an increased irritative action to aggressive factors

TABLE 1

CHEMICAL RELATIONS BETWEEN COMMON IRRITANT DRUGS AND TYPICAL WAR GASES

Aliphatic irritant	Corresponding war gas
Alcohol $H{-}CH_2CH_2{-}OH$	Ethyl dichloroarsine $H{-}CH_2CH_2{-}AsCl_2$
Chloroform $Cl_3C{-}H$	Chloropicrin $Cl_3C{-}NO_2$
Ether $(H{-}CH_2CH_2)_2O$	Mustard gas $(Cl{-}CH_2CH_2)_2S$

associated with altered halogenation and polarity. These war gases usually contain a rather labile halogen, like chlorine or bromine, which, with the hydrocarbon portion, may be considered to be relatively lipoproteophilic with respect to the rest of the molecule. On the other hand, the war gases also contain more potent polarizing radicles, like oxygen, sulfur, arsenic, a nitro group or oxime, which may be relatively hydrophilic or which may reduce the strength of the halogen bond. Differences in relative water-fat solubilities and in ease of hydrolysis may be important factors in the site of action or in the onset or duration of action, as exemplified in the contrast between lacrimators and vesicants.

One theory explaining the action of war gases is on

[1] Proceedings of a Board of the Chemical Warfare Service appointed for the purpose of investigating conditions incident to the disaster at the Cleveland Hospital Clinic, Cleveland, Ohio, on May 15, 1929. Edgewood Arsenal, Maryland, Lieutenant-Colonel Walter C. Baker, C.W.S., commanding. U. S. Government Printing Office, Washington, 1929, 104 pp.

the basis of splitting off halogen, with immediate irritant effect from the resulting halo-acid. This may occur promptly on the wet surfaces of eyes, and of mucous membranes of the nose, mouth, throat and lungs, with such agents as the lacrimators, phosgene and lewisite. On the other hand, as with mustard gas, the partition coefficient may favor absorption into the cells, after which the halogen may split off. The resulting halo-acid within the cell may alter enzyme systems, permeability of the surface membrane or protein equilibria, in such a way as to kill the cell. While such formation of acid may occur, it would have to exceed the buffering capacity of cells and tissues, and this might require relatively large amounts in order to pass the threshold. Neutralization by cellular buffers would be expected to produce the corresponding halide ion which would not markedly affect cellular function. At any rate, exhaustion of the buffer mechanism should reduce further hydrolysis. Direct experiment has shown that molecularly intact mustard gas may be isolated from deep skin layers many hours after absorption. Again, acid injury usually involves protein denaturation and precipitation, whereas war gas injury is characterized more by disturbances of cellular permeability, with swelling, protein hydrolysis and cellular disintegration.[2]

Another type of mechanism of action may operate. This relates to the relatively rigid molecular configuration of the war gas molecule as compared to the cell membrane. The latter is interpreted as a water-lipo-protein interface.[3] Portions of the war gas molecule seem to be relatively lipo-proteophilic, while other portions seem to be more hydrophilic. If enough war gas molecules are present at the cell surface, distortion of the interface may occur. This would result from orientation of the war gas molecule in accordance with the selective affinity of different parts of the molecule for water and lipo-protein, respectively. If this affinity and the interatomic angle forces in the war gas molecules are greater than the surface tension forces which maintain the normal cell surface, torsion may follow, with changes in permeability of the surface film, with resulting swelling and further distortion and strain of the surface membrane. This may comprise the initial inflammatory response to war gases, which may go on to cellular rupture, vascular breakdown, autolysis and necrosis, as so well described by Livingston and Walker.[2] Tight packing of cells, as may be accomplished by high ascorbic acid intake,[4] would tend to reduce the intensity of this reaction, as Livingston and Walker noted.[2]

Whichever mechanism occurs, the prolonged tissue response to war gases would subsequently include the slow removal of necrotic debris, to be followed by gradual repair. In the case of lung irritants, this sluggish process indicates the need for protracted oxygen administration as well as for prophylaxis against psychiatric pneumophobia.

In the biological effects of war gases, therefore, it seems that one or more of the following factors are concerned: (1) relative water, fat and protein solubility, both in transport and in relation to cell surface; (2) relative ease of hydrolysis, with relation to possible formation of halogen acid and the effects of the rest of the molecule; (3) distortion of cellular surfaces due to the molecular configuration of war gas molecules or to their secondary valence forces, and (4) effects of war gas molecules on pH, redox potential and colloid, interface and enzyme equilibria.

As in the case of sunburn or exposure to poison ivy, once the process of war gas injury is under way, one may hope for benefit only on the basis of symptomatic relief, of aiding the removal of necrotic tissue and of promoting repair. It would seem wise, therefore, to train civilians in "self-aid" in suspected contact with war gas, since first-aid or professional care is apt to be too late.

In order to reduce confusion of thought to a minimum and thus to help prevent panic in suspected attack with war gas, "self-aid" should be devised in as simple a manner as possible. Recommendations should be based on the least common denominator of effectiveness for whatever is likely to be used by a smart enemy. Since mixtures of war gases are certain to be employed, it seems unwise to worry about specific identification and specific management of potential injury, if such identification is based on such an indefinite procedure as smell.

Absorption of the ordinary war gases and their many obvious chemical relatives may be inhibited by neutralizing hydrolysis, oxidation or adsorption. For civilian use, these methods may be improvised from materials readily available in homes. Since the war gases in general are decomposed or poorly soluble in water, a wet cloth tied over the nose and mouth is a relatively effective barrier to the passage of such vapors, including oil smoke and "nitrous fumes," to the nose, throat and lungs.

The most readily available effective oxidants are the common kitchen bleach solutions, such as "Clorox." These are buffered 3 to 5 per cent. sodium hypochlorite solutions and are non-irritating for blotting the

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[2] P. C. Livingston and H. M. Walker, *British Jour. Ophthal.*, 24: 76, 1940.

[3] J. F. Danielli and H. Davson, *Jour. Cell. Comp. Physiol.*, 5: 495, 1934; J. F. Danielli, *Proc. Roy. Soc.*, B, 121: 605, 1937; A. J. Clark, General Pharmacology, Hndb. Exper. Pharmakol., Erganzungswerk, 4: 14, 1937.

[4] S. B. Wohlbach, *Amer. Jour. Path.*, 9: 689, 1933; J. F. Rinehart, L. D. Greenberg, M. B. Olney and F. Choy, *Arch. Intern. Med.*, 61: 552, 1938.

skin, but should be diluted for application to mucous membranes, for washing the skin or for wetting cloths to breathe through. As is well known, such a solution reacts promptly with mustard gas, 2,2′-dichlorodiethyl sulfide (BP 217° C.), converting it quantitatively to the non-toxic crystalline 2,2′-dichlorodiethyl sulfoxide (MP 110° C.). The use of such sodium hypochlorite solutions for the prevention of mustard gas injury has been widely advertised in England.[5] Confirmation of their effectiveness against both mustard gas and lewisite has been obtained by Professor T. D. Stewart, of the University of California, Berkeley, on scores of human subjects, and by ourselves on humans and experimental animals. It is immaterial whether oxidation of mustard gas produces the sulfoxide or sulfone, or further decomposition, or what is produced on treating lewisite with hypochlorite. Direct experiment shows that such treatment of these compounds or their obvious chemical relatives results in non-toxic residues.

For alkaline hydrolysis, sodium bicarbonate solutions around 2 per cent. may be readily prepared in a black-out room by dissolving a teaspoonful of baking soda in a glass of water. Such a solution is helpful in washing out the eyes, nose and throat in suspected war gas irritation, or for wetting cloths to breathe through.

The most suitable and readily available detergent adsorbent is lather from ordinary soap and water or soap flakes or tincture of green soap. This is particularly useful, as are hypochlorite solutions, in preventing skin injury from suspected contact with blister gases. The data in Table 2 show the value of soap and hypochlorite in reducing skin injury (in a rather sensitive test object) from mustard gas application, in comparison with such a mustard gas solvent as kerosene.

The common blister gases are soluble in kerosene, gasoline, acetone, carbon tetrachloride and similar fat solvents. During World War I, it was naturally assumed that such solvents would be useful in removing liquid blister gas splashes from the skin. We have found no data to support this idea. However, current advice to civilians retains this recommendation. It is to be remembered that kerosene, gasoline and acetone may be absorbed through the skin, and that, like carbon tetrachloride, they are themselves skin irritants. They are also solvents of low viscosity and tend to spread easily. It is unlikely that they would be used carefully under the conditions of excitement existing in the crisis of suspected war gas contact. Our experiments show (Table 2) that even under controlled conditions they are much less satisfactory than lather or hypochlorite.[6]

Pharmacologists have the obligation of establishing and explaining the facts regarding the action of chemicals on living things. They have the privilege of applying such information to whatever practical problem may be appropriate. With respect to war gases, present pharmacological information suggests that the simplest and most effective advice for civilian protection against such gases might be: (1) obey air-raid rules, taking refuge during an alarm in an air-raid shelter or black-out room, with doors and windows shut and the windows screened or heavily curtained on the inside to prevent injury from flying glass, if bombing occurs; (2) if the shelter is broken open by bombing, and if war gases are suspected by fogs, peculiar odors, smarting or stinging in the eyes, nose or throat, or by coughing, sneezing or gasping, or by any other suspicions, tie a cloth soaked in baking-soda solution, or diluted kitchen bleach solution, over the nose and mouth to breathe through,

TABLE 2

AVERAGE CHARACTER OF SKIN RESPONSE IN RABBITS TO 0.05 CC 10 PER CENT. MUSTARD GAS (HS) IN ETHER, WITH TREATMENT CONSISTING OF THRICE BLOTTING AREA OF APPLICATION (ROUGH CIRCLE 10 MM IN DIAMETER) ONE MINUTE AFTER APPLYING HS WITH GAUZE SOAKED IN KEROSENE, SOAP AND WATER, OR 3 PER CENT. NaOCl (CLOROX), RESPECTIVELY*

Day	Untreated	Kerosene	Soap	3 Per Cent. NaOCl
1	Intense erythema and edema	Moderate erythema, slight edema	Diffuse erythema, slight edema	Diffuse erythema
2	Diffuse erythema and edema, central blanched area	Diffuse erythema and edema, central blanched area	Blanched area, 10 × 15 mm	Blanched area, 10 × 15 mm
5	Deep hemorrhagic necrotic area, 10 × 12 mm	Hemorrhagic necrotic area, 12 × 15 mm, with diffuse necrosis at edges	Thin scaley necrosis, 8 × 10 mm	Thin scaley necrosis, 8 × 10 mm
15	Heavy adherent scab, 10 × 12 mm	Broad adherent scab, 15 × 20 mm	Thin flakey scab, 8 × 10 mm	Thin flakey scab, 8 × 10 mm
22	Heavy adherent scab, 10 × 12 mm	Broad adherent scab, 15 × 20 mm	Light scar	Light scar

* No significant difference from untreated areas observed after application (as above) of either 3 per cent. H_2O_2, acetone or "bleach paste." Treatment with 5 per cent. NaOH in 30 per cent. glycerine seems to increase inflammatory reaction during first week, producing a deeper and slower healing necrotic area. Ten per cent. benzoyl peroxide in nona ethylene glycol seems to have little effect on HS reaction during first day or so, but seems to reduce necrotic reaction and time required for healing. However, 10 per cent. benzoyl peroxide in talc affords no protection when dusted on skin previous to exposure. Observations similar to the above have been obtained with lewisite; healing, however, is more rapid.

[5] Half-page advertisement *British Med. Jour.*, opposite page 445, April 4, 1942.

[6] D. F. Marsh and C. D. Leake, *Calif. West. Med.*, 57: 8, 1942. Acknowledged in spite of printer's many typographical errors!

keep it wet, shut one eye and squint through the other, and lie down with head in arms; (3) if eyes, nose or throat are irritated, wash them with a solution of a teaspoonful of baking soda in a glass of water; (4) if splashes of liquid are suspected on the skin or clothes, throw the outer clothing out the window, blot the skin splash promptly and repeatedly with a cloth wet with kitchen bleach solution, lather thoroughly and frequently with soap and rinse copiously with water. If subsequent injury results, the management is symptomatic at a casualty station or hospital.

These considerations were fully reviewed early in 1942 by the San Francisco and Alameda Committees on the Medical Aspects of War Gases. Special discussions along these lines have been widely published on the West Coast for civilian information.[7] Experience has shown that these suggestions for "self-aid" in handling suspected war gas exposure are appreciatively received by the public because they are simple and sensible. Recently these suggestions in substance have been included in "official" recommendations.[8]

OBITUARY

JACOB GOULD SCHURMAN
1854–1942

The death of Jacob Gould Schurman at the ripe age of eighty-eight years will remind present-day scientists of the versatility of their colleagues in an earlier generation. Dr. Schurman was trained as a philosopher in a day when to be such was to qualify both as a metaphysician and moralist and also as a mental scientist. When, in 1903, the first selection of distinguished men was made from those listed in the first edition of "American Men of Science," Dr. Schurman's name received a "star" among the fifty leading psychologists of that time. He had already served eleven years as president of Cornell University, but was still rated by his colleagues as an active scientist and member of the American Psychological Association.

Dr. Schurman's long career was marked with distinction as a scholar and teacher, as a university administrator and as a diplomat. As dean of the Susan Linn Sage School of Philosophy, which was established at Cornell by a trustee, Henry W. Sage, in memory of his wife, Dr. Schurman saw to it that one of the chairs in this school should be devoted to the new science of psychology. The first incumbents, Frank Angell, followed after one year by Edward Bradford Titchener, were brought to Cornell by President Schurman from the psychological laboratory of Wilhelm Wundt in Leipzig. Thus, from the beginning of the school, experimental research in psychology was fostered and developed by its dean and president.

Academic men of science also owe a debt of gratitude to this president of Cornell for his promotion of faculty participation in university administration. It was under Dr. Schurman's régime that faculty representatives were first elected to the board of trustees of Cornell University, and it was likewise with his support that the faculty of the College of Arts and Sciences was granted opportunity to elect its own dean. In all matters of university policy Dr. Schurman was well in advance of his time. If the elective deanship failed to perpetuate itself at Cornell, it was for lack of faculty enterprise and not for lack of support by the president.

The foundation and endowment of the Cornell Medical College owe much to Dr. Schurman, and the advancement of experimental science at Cornell was always of first importance to him. It was under his leadership that the university acquired three of its outstanding laboratories: Stimson Hall for the promotion of the medical sciences; Rockefeller Hall for the promotion of physics, and the well-planned and equipped Baker Laboratory of Chemistry.

After thirty-four years at Cornell, including twenty-eight as president of the university, Dr. Schurman retired to carry on a political and diplomatic career already initiated by his appointment in 1899 as president of the first United States Philippine Commission. Yet his interest in academic matters never lapsed. He was the leading spirit in raising an endowment of one-half million dollars for the University of Heidelberg—a university in which Dr. Schurman himself, like many other American scholars, had received training. He also lectured frequently before academic audiences, including appointments in 1931 and 1932 as honorary lecturer on international relations at the Institute of Technology in Pasadena, California.

Men of his breadth of view and depth of knowledge are rare to-day. To be a great educational leader and at the same time to be recognized as a participating member of several cognate fields of learning, is a distinction which can no longer be claimed by a specialist. Yet it is to men like Dr. Schurman that we owe the foundations and endowments which have made modern scientific progress possible, and our debt to them is greater than we are likely to remember.

R. M. Ogden

Cornell University

[7] Articles on war gases by J. F. Hildebrand (*The Commonwealth*, 1942; *San Francisco Chronicle*, Feb. 15, 1942), M. Silverman, *San Francisco Chronicle*, March 15, 22, 29, Apr. 5, 1942) and W. F. Mould, leading West Coast newspapers through June and July, 1942.

[8] *Jour. Am. Med. Assn.*, 119: 889, July 11, 1942.

DEATHS AND MEMORIALS

ALBERT W. SMITH, professor of mechanical engineering at Stanford University from 1892 to 1904; later successively director of Sibley College of Engineering of Cornell University and dean of the college, died on August 16 in his eighty-sixth year.

DR. LOUIS ROULE, professor of science at Toulouse University from 1885 to 1910, later professor at the Paris Museum of Natural History, died on August 4 at the age of eighty-one years.

THE astronomical observatory of Vanderbilt University, founded over sixty years ago, will hereafter be known officially as "Barnard Observatory of Vanderbilt University" in honor of the late Edward Emerson Barnard, the distinguished astronomer who was an alumnus of the university.

SCIENTIFIC EVENTS

THE NATIONAL PARKS ASSOCIATION

THE following resolutions were adopted at the annual meeting on May 15 of the trustees of the National Parks Association:

COMMERCIAL ENCROACHMENTS

Since the National Parks and Monuments comprise a valuable part of the heritage which we are now fighting to maintain, and

Since pressure was exerted during the first world war for such destructive and depleting uses as grazing, timber cutting and power development in the National Parks, and

Since increasing pressure for similar encroachment is being brought upon the National Park Service in the present war, be it therefore

Resolved, That the National Parks and Monuments should not be opened to any commercial use until there is definite proof of its necessity, and until all other possible sources of the needed materials have been explored, and be it further

Resolved, That the National Parks Association will examine each threat of commercial encroachment upon the National Parks and Monuments to determine whether it is inimical to the public interest.

THE QUARTERING OF ENEMY ALIENS IN NATIONAL PARKS

Since the proposed quartering of enemy aliens within the National Parks and Monuments would jeopardize the natural conditions, particularly in forested areas, which are subject to destruction by fire, and

Since such quartering of enemy aliens would certainly interfere with normal use by visitors seeking rest and inspiration therein, be it therefore

Resolved, That enemy aliens should be quartered in areas other than the National Parks and Monuments and where they will not endanger the war effort.

MILITARY USE OF NATIONAL PARKS AND MONUMENTS

Since the National Primeval Parks and National Monuments were established as outstanding natural areas worthy of complete preservation for the benefit and enjoyment of the people, and

Since extensive military training and maneuvers are incompatible with such use of these areas, and irreparable damage to their natural features must result therefrom, and

Since less restricted and equally suitable areas on other public lands are available for military purposes, be it

Resolved, That only in case of proven necessity, and after every other possible area has been investigated and shown to be unsuitable for the proposed use, and only in accordance with the recommendation of the National Park Service and the Department of the Interior, should National Primeval Parks and National Monuments be used for military purposes.

THE VIRGIN FOREST OF THE PORCUPINE MOUNTAINS

Since the virgin forest of the Porcupine Mountains on Michigan's upper peninsula constitutes the finest remaining example of the original forests in the Great Lakes region, and

Since there is imminent danger of these mountains being desecrated through reckless and wasteful lumbering or development for extensive tourist use with the resultant loss of their value as a superlative natural area, be it therefore

Resolved, That the Porcupine Mountains should be acquired by the Federal Government for preservation in their present primitive condition.

SABOTAGE FOREST FIRE CONTROL

Since the probabilities of subversive action in setting forest fires present a serious danger to the nation's heritage of superlative natural areas, and to the prosecution of the war, be it therefore

Resolved, That advance provision of adequate funds should be made for the purpose of preventing and combating such forest fires.

THE PENNSYLVANIA STATE FORESTS

DR. GIFFORD PINCHOT, formerly Pennsylvania State Commissioner of Forestry and forester of the Department of Agriculture; Governor of Pennsylvania from 1923 to 1927 and from 1931 to 1935, has made public the following statement:

In a letter to Harrisburg I said that I had recently seen portions of the state forests of Pennsylvania butchered by lumbermen, and urged that it be stopped.

Harrisburg refused to stop it, and quoted in defense two men without professional training or practical experience in forestry. One of them set up our war needs in excuse. That excuse is worthless.

If the war needed every last tree in Pennsylvania, we should give it, of course. But the war does not need it.

The chief forester of the United States Forest Service

says this: "I am convinced that in winning the war it is wholly unnecessary, and in addition the worst possible public and industrial policy, to destroy or depreciate the future productivity of our forests. We can cut all the timber we need to meet every conceivable war requirement and still cut in such a way that the productivity of the forest will be increased rather than impaired."

The productivity of our state forests is being impaired. Within the last two years the most destructive cutting of them ever perpetrated has been and is still going on.

This cutting, which Harrisburg defends, is not limited to trees selected and marked, as good forestry requires, but all trees above certain sizes have been sold and cut, without discrimination.

Trees too young for cutting, trees needed for seed, or to maintain the forest cover, help control floods, prevent erosion or otherwise necessary, have been cut regardless.

The second Harrisburg witness without professional training or practical experience alleged that this is good forestry. I say it is not forestry at all, but forest butchery. For the safety and welfare of Pennsylvania, it ought to be stopped. Will you help stop it?

THE BEACH PLUM PRIZES OF THE ARNOLD ARBORETUM

Dr. James R. Jewett, of Cambridge, Mass., emeritus professor of Arabic, Harvard University, in 1940 presented the Arnold Arboretum with a capital sum under the conditions that from its income two annual prizes might be awarded to individuals who have made significant contributions to the improvement of the native beach plum, or who, through the development of beach-plum products, may have made contributions of social significance. The first awards were made in 1941.

The James R. Jewett Prize of $100 for 1942 has been awarded to J. Milton Batchelor, of the U. S. Soil Conservation Service, for his outstanding work with the native beach plum. The Vieno T. Johnson Prize of $50 has been awarded to William Foster, of East Sandwich, Mass.

The committee of selection was made up of staff members of the Arnold Arboretum, the Massachusetts State College and a representative of the Cape Cod beach plum growers. The recognition of the work of a professionally trained plant hunter and a Cape Cod grower as the recipients of the two prizes for 1942 is illustrative of the cooperative spirit now existing in the efforts being made to locate and to propagate the better types of beach plums. At the present time there is much new interest in the beach plum and its products, some of which is directly traceable to an appropriation made last year by the Massachusetts Legislature, providing special funds to the Massachusetts State College for research on beach-plum problems. This bill was the direct result of the continued efforts of Mrs. Wilfred O. White, of Martha's Vineyard, who was the recipient of the James R. Jewett Prize for 1941. Experimental work is now being prosecuted by staff members of the Massachusetts State College, which should eventually solve many problems in reference to selection, propagation, fertilizing, pruning and spraying of the beach plum.

J. Milton Batchelor, the recipient of the James R. Jewett Prize for 1942, was graduated from Cornell University in 1933. For some years he has been a member of the Soil Conservation Service, his particular duties being to find variations in native fruits which might prove to be of economic value, to study their adaptability for use in soil erosion projects and to ascertain their possibilities as ornamentals. His work has involved very extensive travel. On trips to eastern Massachusetts during the past few years he became particularly interested in the beach plum, and has located, propagated and distributed a number of varieties with larger and better fruits. He has freely advised many individuals in Massachusetts who were interested in the beach plum and has vigorously supported the campaign to increase interest in this field.

William Foster, of East Sandwich, Mass., recipient of the Vieno T. Johnson Prize, has for many years been interested in growing beach plums on Cape Cod, and has recently been prominently identified with some of the experimental work now being carried out by members of the horticultural staff of the Massachusetts State College.

THE UNIVERSITY OF MICHIGAN

At his own request, William Gabb Smeaton, professor of chemistry at the University of Michigan, who is now sixty-eight years old, will be retired on September 8. He has been named professor emeritus of chemistry. He served as a member of the faculty of the University of Michigan College of Literature, Science and the Arts for a period of forty years. The following resolution has been adopted by the Board of Regents: "Professor Smeaton has ably and loyally contributed to the successful accomplishment of the university's work through the skilful conduct of instruction, through the preparation of valuable manuals for the use of teachers and students of chemistry and the history of science, and through his participation in the scholarly activities of the institution, and thereby gained for himself the esteem and affection of his colleagues and students which is amply due him as a man of admirable character and recognized ability. . . ."

Walter Bowers Pillsbury, professor of psychology, will retire at the age of seventy years on September 26. He has been named professor emeritus of psychology. He joined the faculty of the university in 1897 and has been associated with the College of Literature, Science and the Arts continuously for forty-five years. The Board of Regents cited Pro-

fessor Pillsbury for the large part he played in the development of the university's department of psychology and for his "noteworthy research, teaching and writing . . . his eminence as a scholar . . . and the genuine affection of students and colleagues inspired by his wholesome character and unassuming friendliness."

Action taken at a recent meeting of the Board of Regents included:

Appointments: Professor Arnold M. Keuthe was appointed acting chairman of the department of aeronautical engineering to take the place of Professor Edward A. Straiker, resigned.

Leaves of absence to staff members called to active military service: John C. Brier, professor of chemical engineering, university year, 1942–43, to serve as lieutenant colonel in the U. S. Army in charge of the Training School at the Ravenna Ordnance Plant at Ravenna, Ohio.

Drs. John M. Sheldon, Edgar A. Kahn, Walter G. Maddock, S. Milton Goldhamer, Moses M. Fröhlich, George Hammond, Harry A. Towsley, Marshall L. Snyder and E. Thurston Thieme, all serving with the U. S. Army Medical Corps in the 298th General Hospital Affiliated Unit.

Dr. Alexander Barry, instructor in anatomy, university year, 1942–43, commissioned in the Air Corps of the U. S. Army.

Dr. Richard C. Armstrong, resident in the department of ophthalmology, university year, 1942–43, commissioned in the U. S. Army Medical Corps.

Dr. Hayden C. Nicholson, associated professor of physiology, university year, 1942–43, commissioned as a captain in the U. S. Army Medical Corps.

Dr. G. Howard Gowen, professorial lecturer in epidemiology, July 9, 1942, to June 30, 1943, called to active duty in U. S. Army.

Steve Remias, instructor in epidemiology, July 15, 1942, to June 30, 1943, called to active duty in the U. S. Navy.

Dr. Herman H. Goldstine, instructor in mathematics, July 18, 1942, to June 30, 1943, for service as a First Lieutenant in the U. S. Army Air Forces.

Professor Harley Bartlett, chairman of the department of botany, university year, 1942–43, to carry on investigations for the U. S. Department of Agriculture.

Dr. James M. Cork, professor of physics, summer of 1942, to take part in the research program at the California Institute of Technology of adapting the cyclotron to war purposes.

Dr. L. H. Newburgh, professor of clinical investigations in the department of internal medicine, June 1, 1942, to December 1, 1942, to become a member of a subcommittee on clinical investigations for the Division of Medical Sciences of the National Research Council and to devote his entire time to medical problems arising out of the war.

Dr. Robert C. F. Bartels, instructor in mathematics, June 15, 1942, to June 14, 1943, to serve as a consulting mathematician in the Bureau of Navigation, U. S. Navy.

H. S. Bull, assistant professor of electrical engineering, university year, 1942–43, to engage in research for the U. S. Army Signal Corps.

Edwin M. Baker, professor of chemical engineering, summer term, to devote full time to work for the Houdaille-Hershey Corporation and other companies on the manufacture of armaments.

Dr. Clarence A. Siebert, associated professor of metallurgical engineering, summer term, to carry on work with the Houdaille-Hershey Corporation related to the war program.

Lewis N. Holland, assistant professor of electrical engineering, summer term, to term defense courses.

Arthur J. Decker, professor of civil engineering, summer term of 1942.

William S. Housel, associate professor of civil engineering, summer term of 1942.

Extensions of Leave: The leave of absence of Professor Ralph A. Sawyer, of the department of physics, has been extended for the university year 1942–43. Professor Sawyer is a lieutenant commander in the U. S. Navy in charge of the testing laboratory at the Naval Proving Grounds at Dahlgren, Va.

SCIENTIFIC NOTES AND NEWS

THE Royal Society of Canada has awarded the Flavelle Medal "for original research of special and conspicuous merit" to Dr. J. H. Craigie, head of the Dominion Rust Research Laboratory at Winnipeg, Man., in recognition of his work on the control of wheat rust.

AT the annual meeting of the Woods Hole Marine Biological Laboratory on August 11, Lawrason Riggs was elected president of the corporation and chairman of the board of trustees to succeed Dr. Frank R. Lillie, who was made president emeritus. The newly created position of vice-president was filled by the election of Dr. E. Newton Harvey, professor of physiology at Princeton University.

AT the annual meeting of the trustees of the Oceanographic Institution, Woods Hole, Dr. Alfred C. Redfield, professor of physiology at Harvard University, was elected associate director.

A PORTRAIT of Dr. John Bentley Squier, professor emeritus of urology of Columbia University College of Physicians and Surgeons, was unveiled on July 1 at the Squier Urological Clinic of the Presbyterian Hospital. The portrait, the work of Julian Lamar, is a bequest of the late Adolph S. Ochs, publisher of *The New York Times* from 1896 to 1935.

DR. ARTHUR J. HILL, chairman of the department of chemistry and director of the Sterling Laboratory of Yale University, has been appointed to the new Whitehead professorship in chemistry. The Whitehead professorship was named in honor of the late

Conkey P. Whitehead, of the class of 1919, who died in 1940, leaving a bequest to the university for the support of work in chemistry.

Dr. Baldwin M. Woods, professor of mechanical engineering at the University of California, Berkeley, has been named director of university extension. Boyd B. Rakestraw, assistant director, who has been in charge of extension activities since the retirement of Professor Leon J. Richardson four years ago, has become associate director.

Dr. Catharine Macfarlane, professor of gynecology, has been made research professor of gynecology at the Woman's Medical College of Pennsylvania in recognition of her work in cancer research.

Dr. A. Castiglioni, formerly professor of the history of medicine at Padua, is giving a series of weekly lectures on medical history at the Yale University School of Medicine.

Sir Henry Tizard, since 1929 rector of the Imperial College of Science and Technology, London, known for his researches in aeronautics, has been elected president of Magdalen College, Oxford. *Nature* points out that this is a timely and important break with Oxford tradition, for he is the first man of science to become the head of a college there. Sir Henry is now a member of the British Air Council and of the Advisory Council of the Ministry of Aircraft Production.

Dr. Myron E. Wegman has been appointed director of training and research in the Bureau of Child Hygiene, New York City. A training unit has been established at the Kips Bay-Yorkville Health Center, 411 East Sixty-ninth Street, which, under his direction, will train new physicians employed by the bureau to replace staff members called into military service.

A. E. White, director of the department of engineering research and professor of metallurgical engineering at the University of Michigan, has been nominated as manager of the American Society of Mechanical Engineers for 1943.

F. C. Todd, of the Pennsylvania State College, has joined the technical staff of Battelle Memorial Institute, Columbus, Ohio. He will undertake research work in industrial physics.

Dr. Leonard N. Allison, fish pathologist and district fisheries biologist of the Institute for Fisheries Research of the Michigan Department of Conservation, has joined the staff of the State Fish Hatchery, Grayling, Mich.

Dr. Paul Herget, assistant professor of astronomy at the University of Cincinnati and astronomer at the Cincinnati Observatory, has leave of absence for the duration of the war to accept a war emergency appointment to the Nautical Almanac Office of the U. S. Naval Observatory, Washington.

Dr. Frank L. Campbell, professor of entomology at the Ohio State University, has leave of absence to perform advisory service on insecticides in the Chemicals Division of the Office for Agricultural War Relations of the U. S. Department of Agriculture.

Oliver Bowles has been named chief of the Nonmetal Economics Division of the U. S. Bureau of Mines, succeeding Paul M. Tyler, who has become a member of the Board of Economic Warfare.

Sir Guy Marshall, who has been director of the British Imperial Institute of Entomology since its foundation in 1911, retired on July 31. Dr. S. A. Neave has succeeded him.

The appointment of a committee of chemists and chemical engineers to advise the Government on technical processes is announced by Ernest W. Reid, chief of the Chemicals Branch of the War Production Board. The committee will pass upon the relative merits of competing chemical processes involved in the war effort. The basis upon which the findings will be made is (a) which process can be placed in production soonest and (b) which uses the smallest amount of critical materials. Donald B. Keyes, head consultant to the branch and professor of chemical engineering at the University of Illinois, is chairman of the committee. The members are Marston T. Bogert, Joel H. Hildebrand, S. C. Lind, Frank C. Whitmore, Gustavus J. Esselen, Carl S. Miner, Foster D. Snell, Charles C. Brown, Charles R. Downs, Sidney D. Kirkpatrick and Fred H. Rhodes.

A committee has been formed in the British House of Commons to consider the question of synthetic rubber to be constituted as follows: F. W. Bain, chairman of the Chemical Control Board of the Ministry of Supply, *chairman;* Sir Edward V. Appleton, secretary of the Department of Scientific and Industrial Research; Dr. J. W. Armit, director-general of explosives at the Ministry of Supply; Sir Robert Robinson, Waynflete professor of chemistry at the University of Oxford; and Dr. F. Roffey, controller of chemical research at the Ministry of Supply.

The British Government was on July 16 requested by an influential deputation, composed of scientific men, members of Parliament and peers, which was arranged by the War Cabinet Scientific Advisory Committee, to set up a full-time scientific and technical joint board. This would have as its aim the fullest strategic use of scientific man-power and resources and the proper organization and exchange of scientific and technical information relating to the

war effort. Members of the deputation included Lord Samuel, Captain Leonard Plugge, M.P. (chairman of the Parliamentary and Scientific Committee, from whom the deputation came), Dr. W. Wooldridge, C. S. Garland (British Association of Chemists), Professor W. Makower (Institute of Physics), Sir Lawrence Bragg, Professor B. W. Holman, Gower Pimm (Institute of Structural Engineers), Professor Bernal (Association of Scientific Workers), Colonel Thompson (president of the Institution of Mechanical Engineers), J. H. Wootton-Davies, M.P., Lord Pentland, Hugh Linstead, M.P., R. B. Pilcher (Institute of Chemistry), Lord Leverhulme and Lord Hinchingbrooke. It is reported that one of the points emphasized by some members of the deputation was that young scientific men of ability should be given more encouragement to exercise their inventive faculties. The view was expressed that not only the War Cabinet but the Chief of Staffs Committee should be advised by scientific men on appropriate matters.

IT is reported in *Nature* that at a recent meeting of the trustees of the Beit Memorial Fellowships for Medical Research, Dr. A. N. Drury, Huddersfield lecturer in special pathology in the University of Cambridge, was appointed to the advisory board in succession to the late Professor A. J. Clark. The trustees noted the election this year of three past fellows to the fellowship of the Royal Society, namely, E. Hindle (junior fellow, 1910–12, and senior in tropical medicine, 1927–33), F. M. Burnet (1926–27) and A. R. Todd (1935–36). Of the twenty-eight present fellows, there are now fourteen seconded for whole-time war-work. The following elections have been made, with permission for each fellow to be seconded at any time for war duties: *4th Year Fellowship* (£500 a year), E. G. L. Bywaters, to continue his studies of crush injuries in relation to kidney function, at the British Postgraduate Medical School, London. *Junior Fellowships* (£400 a year), Dr. D. Herbert, to study the biochemistry of toxoids for active immunization against gas gangrene, at the Dunn Biochemical Laboratory, University of Cambridge. Dr. F. W. Landgrebe, to study the separation of posterior pituitary hormones and their clinical uses, at the Medical School, University of Aberdeen.

THE seventeenth Congress of the French Medical Association of North America will be held at the Hôtel Mont-Royal, Montreal, from September 14 to 17.

THE London correspondent of the *Journal* of the American Medical Association states that the report on the work of London University during the past year shows that in spite of financial and other difficulties due to the war it remains a valuable institution which is producing skilled men and women both for war work and for playing a useful part in reconstruction after victory. In 1938–1939 there were 14,587 internal and 10,893 external students. In 1940–1941 (the first complete war year) the figures were 8,916 and 8,840. The smaller diminution on the external side is explained by the fact that evacuation has not hit it as much as it has dislocated the collegiate side. Moreover, many serving members of the armed forces are pursuing courses of study as external students. The figures for 1941–1942 are not yet complete, but according to the *Journal* there appears to be a slight increase in both internal and external students. In the latter it is in faculties whose work is most directly related to the war effort—science and engineering—that numbers are best maintained. Turning to students attending schools of the university, there is a sharp distinction between the medical and non-medical schools. In 1940–1941 medical students were nearly 90 per cent. of the number for 1938–1939, while non-medical students were only 56 per cent. Before the war 63 per cent. of the students at non-medical schools were men; now the proportion is only 50 per cent. In the medical schools the proportion of 90 per cent. has scarcely changed. The main new problem during the year has arisen from the government's decision to call up women for national service, which has had an immediate effect on the position of women students.

DISCUSSION

THE PRODUCTION OF TWO ANTIBACTERIAL SUBSTANCES, FUMIGACIN AND CLAVACIN

THE successful utilization of penicillin, produced by the fungus *Penicillium notatum,* for combating certain human diseases resistant to other treatments has focussed attention upon the possibility that various other fungi isolated from such natural substrates as soil or manure might produce different antibiotic substances. These might possibly supplement penicillin by acting upon pathogens not affected by this substance. Chemical compounds might thus be obtained which possess totally different antibacterial mechanisms. Several fungi, other than *P. notatum,* have already been shown to produce antibiotic substances; some of these have been isolated in crystalline form and identified chemically, whereas others have been obtained only in a concentrated active form.[1] In a study of the presence of antagonistic fungi in nature, the bacteria-enriched agar media[2] have been utilized.

[1] H. Raistrick and G. Smith, *Chem. Ind.*, 60: 828–830, 1941; A. E. Oxford, H. Raistrick and G. Smith, *ibid.*, 61: 22–24, 48–51, 1942; E. C. White, SCIENCE, 92: 127, 1940; G. A. Glister, *Nature*, 148–470, 1941.

[2] S. A. Waksman and H. B. Woodruff, *Jour. Bact.*, 40: 581–600, 1940.

More than 160 cultures of antagonists were thus isolated from soils, manures and composts.[3] These fungi were divided into nine groups on the basis of their taxonomic and physiologic relationships and were found to vary greatly in their capacity to produce antibacterial substances.

Of these antagonistic fungi, two species of *Aspergillus* were studied in greater detail: *A. fumigatus,* of which 16 strains were isolated from different soils, and *A. clavatus,* represented by 3 strains isolated from stable manure. In synthetic media, these two organisms produced active substances, that differed greatly in their chemical nature and in biological activity. These two substances were designated as *fumigacin* and *clavacin,* respectively.

Fumigacin is readily soluble in chloroform and in ethyl alcohol and to a limited extent in ether and in water; it precipitates from an alcoholic solution, on cooling, as fine, long, needle-shaped crystals. The substance is active against gram-positive bacteria but has only limited activity against gram-negative forms, as represented by *Salmonella* and the colon-aerogenes groups. Fumigacin is isolated from the medium by adsorption on norit, and subsequent elution with chloroform, after preliminary treatment of the norit with ether. The chloroform is removed by distillation and the active substance is dissolved in alcohol. Fumigacin is markedly different from the pigment fumigatin, isolated by Raistrick and associates,[4] in its mode of formation, chemical properties and biological activity.[5]

Clavacin is soluble in ether, chloroform, alcohol and water. As yet, it has not been isolated in crystalline form. It can be extracted from the culture medium by direct treatment of the culture filtrate with ether and chloroform, or it can first be adsorbed on norit and then removed from the latter by means of these solvents. It is readily soluble in dilute alkalies. Clavacin is particularly active against gram-negative bacteria, the colon-aerogenes group being nearly as sensitive as staphylococci and spore-forming bacteria. Another important characteristic of this substance is its high bactericidal property. It is known that most antibiotic substances act upon bacteria primarily as a result of their bacteriostatic properties; they are rather weakly bactericidal. Clavacin appears to be distinct from these in this respect, possessing both high bacteriostatic and high bactericidal properties, 6 to 18-hour-old cultures of various gram-negative and gram-positive bacteria being killed within 2 to 6 hours by dilution of 1:50,000 to 1:500,000 of the crude clavacin.

The substance recently isolated by Wiesner[6] from *A. clavatus* appears to be similar to clavacin, if not identical with it.

Selman A. Waksman
Elizabeth S. Horning
Ernest L. Spencer

New Jersey Agricultural Experiment
Station, Rutgers University

[3] S. A. Waksman and E. S. Horning. In press.

[4] W. K. Anslow and H. Raistrick, *Biochem. Jour.,* 32: 687–696, 1938; A. E. Oxford and H. Raistrick, *Chem. Ind.,* 61: 128–129, 1942.

[5] S. A. Waksman, E. S. Horning and E. L. Spencer. In preparation.

[6] B. P. Wiesner, *Nature,* 149: 356–357, 1942.

NATURAL PROTECTION AGAINST SUNBURN

Every one knows that skin which has been exposed to sunlight is less likely to sunburn than skin that has not been exposed. However, the explanation usually assigned is only partially correct at best. Skin which has been exposed ordinarily assumes a brown or tan color, principally due to the formation of melanin pigment,[1] and Finsen[2] about 1900 suggested that this pigment acts as an effective screen to mitigate the action of the sun's rays. This explanation seems so logical that it has been almost universally accepted. However, the pigment is located principally in the basal cell layer of the epidermis, whereas findings subsequent to Finsen's show that the cells primarily affected in sunburn are chiefly the prickle cells which lie superficial to most of the pigment. This arrangement of the pigment is characteristic of white skin, whereas in Negro skin it is more evenly distributed throughout the epidermis.

About 1927 Guillaume[3] suggested that the thickening of the corneum or horny layer of the epidermis might be the principal protective factor, *i.e.,* the thickening of this layer should decrease the amount of radiation penetrating to the cells beneath. This suggestion was followed up by Miescher,[4] who showed that sufficient thickening of the corneum occurs after exposure to sunlight to provide effective protection.

In the disease, *vitiligo,* certain areas of the skin do not produce pigment, but exposure of these areas to ultraviolet radiation causes a decrease in sensitivity to subsequent exposure.[5] This is further evidence that pigment is not the sole protective agent.[6]

[1] See E. A. Edwards and S. Q. Duntley, Science, 90: 235, 1939.

[2] N. R. Finsen, *Mitt. Finsens Med. Lysinstitut,* 1: 8, 1900.

[3] H. C. Guillaume, "Les Radiations Lumineuse en Physiologie et en Therapeutique," Paris, Masson et Cie, 1927.

[4] G. Miescher, *Strahlentherapie,* 35: 403, 1930.

[5] C. With, *British Jour. Dermatol. and Syph.,* 32: 145, 1920.

[6] For additional discussion and references see: F. Ellinger, "Radiation Therapy," New York, Elsevier Publishing Company, 1941; H. F. Blum, "Photodynamic Ac-

Demonstration that the transmission of the sunburn-producing wave-lengths by the epidermis of the albino mouse is greatly decreased by exposure of the animal to such radiation adds further evidence.[7]

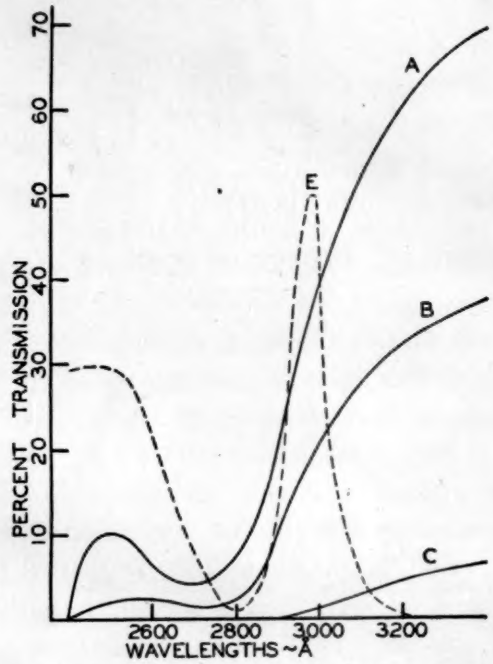

FIG. 1. A: Transmission of normal epidermis of albino mouse ear. B; Transmission of epidermis of ear of albino mouse exposed to ultraviolet radiation for 31 weeks. C; Transmission of well-pigmented epidermis of forearm of man. E; action spectrum of erythema of sunburn of man. This curve is not accurately established for the mouse but has approximately the same long wave-length limit.

These animals do not, of course, form melanin pigment, and hence the decreased transmission of the epidermis must result from some other change. The horny layer is thickened in the exposed animals, and this offers the most probable explanation for the decreased transmission. Fig. 1 illustrates this change in transmission in the region of wave-lengths that cause sunburn, together with curves of transmission by human epidermis.

None of this evidence completely rules out melanin as a factor in protection against sunburn. It shows, however, that it is not the only factor, and probably not the major one in the case of white skin. The melanin must function effectively in preventing penetration of the radiation below the epidermis, which may be of considerable importance in determining the site of cutaneous cancer.[7]

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NATIONAL INSTITUTE OF HEALTH,
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tion and Diseases Caused by Light,'' New York, Reinhold Publishing Corporation, 1941.

[7] J. S. Kirby-Smith, H. F. Blum and H. G. Grady, *Jour. Nat. Cancer Inst.*, 2: 403, 1942.

THE LISTING OF MEDICAL SCHOOLS

MAY I be permitted, as one long interested in collegiate statistics, to point out what I consider an unfortunate aspect of the article "Research Activity and the Quality of Teaching in Medical Schools," by Dr. Albert E. Casey, of the Louisiana State University, published in SCIENCE for July 31, 1942. I shall not discuss the validity of state board medical examinations as a criterion for the quality of medical teaching. I do wish to comment upon the publication in 1942 of a listing of medical schools based upon articles by faculty members appearing in medical journals from March, 1932, to March, 1934. The use of statistics which date back eight years or more to another decade is by no means justified by the back-handed statement that "Sufficient time has elapsed so that the standing of the schools need not necessarily be that of 1934."

The years since 1932–34 have been a period of notable personnel changes in medical faculties of the schools listed and consequent changes in research activity. For example, at the College of Medicine of the University of Cincinnati, our records show that the publications of research for the calendar years 1940 and 1941 are approximately twice those for the years 1932 and 1933. It is my impression that there have been similar advances at Duke, Vanderbilt, Louisville and other medical schools. To sum up, my fear is that Dr. Casey's listing of medical schools, based on old data, will be popularly quoted as representing their present status in respect to research activity and publication.

RAYMOND WALTERS
UNIVERSITY OF CINCINNATI

THE SHOT-PUT AND THE EARTH'S ROTATION

IN a most estimable weekly magazine having a circulation of millions is a department designed to enable its readers to keep up with the world. Once the editor of that department assured us that mercury poured into an open dish remained undiminished in weight, as though mercury gave off no vapor. Recently that department assured us that on account of the earth's rotation an athlete can put the 16-pound shot farther toward the east than toward the west. We are skeptical, for although it is quite true that the athlete while hurling the shot toward the east is moving toward the wished-for mark with a velocity of about 17 miles per minute, the mark at which he aims is moving away from him with that same velocity, with the net result that his shot-put is precisely the same as though the earth were standing still; similarly, if he puts the shot toward the west. Since a body moving south gradually grows lighter his put toward the south might per-

haps exceed his northward put by the thousandth part of a micron.

If the athlete is determined to utilize the earth's rotation in beating the present record of about 56 feet he should go to a theological seminary and learn how the prophet Joshua in his blitzkrieg against the Amorites made sun and moon stand still by stopping the earth's rotation. Armed with this knowledge, he could, immediately after putting the shot toward the east, stop the earth's rotation, and have the satisfaction of beating the record by several miles.

Joseph O. Thompson

Amherst College

STATEMENT

In my radio address printed in Science for July 3, 1942, I used a phrase commencing: "Frequently we become conscious of the philosophy of the old darky. . . ." It has come to my attention that the use of the word "darky" is likely to hurt the feelings of members of the Negro race. I need hardly say that anything approaching an unkindly wording was farthest from my intention, and I am deeply grieved that the wording I used may have caused offense. Being unfamiliar with the implications involved in the word "darky," I used that designation as conveying to the mind, for the purposes of my illustration, the lovable characteristics of an individual who might never have had the opportunity of a formal education but had, nevertheless, thought much of his own accord and, endowed with a certain richness of experience in life, had come to philosophize in a really profound manner upon certain situations arising out of that experience. I never liked the word "Negro" as it sounded harsh and discriminatory, and I used the designation "darky" in the same way as I might say: "There was a canny old Scot who remarked. . . ."

Again may I express my very deepest regret at the unfortunate implication contained in my words, which I am sure my many friends in the Negro race, and particularly those in my own profession, will realize were uttered without any thought that they could hurt the feelings of a race for which I have the warmest regard.

W. F. G. Swann

QUOTATIONS

WAR METALLURGICAL RESEARCH

Frank B. Jewett, president of the National Academy of Sciences, announces that the academy's Metals and Minerals Advisory Committee for the past 18 months has furnished OPM and WPB with 113 reports. Fifty-three of these were on metals substitution and conservation, 47 on ferrous minerals and ferroalloys, 4 on tin smelting and reclamation, and 9 on nonmetallic minerals. These reports, prepared by the various subcommittees of the Advisory Committee, dealt principally with problems arising from the necessity for allocation and substitution of materials, not only for general civilian uses, but even more particularly for war production processes and increased production of war materials.

The work of this advisory committee, according to Dr. Jewett, has been greatly enlarged since Pearl Harbor and is to be further increased as it functions with and for the new War Metallurgy Committee. Clyde Williams, director of Battelle Memorial Institute, Columbus, Ohio, and chairman of the advisory committee, is also chairman of the new War Metallurgy Committee which has primarily been set up to appraise and conduct needed research work for the Army, the Navy and other governmental departments as well as industry. This committee is composed of 26 members, the advisory committee of 63 regular members, plus special members, and 20 other specialists frequently are called in for advice on specific problems. Associations and technical societies are also taking an active part in the problems of metallurgical reports and research.

It is the function of the War Metallurgy Committee to collect data and information as requested by either the WPB or the Office of Scientific Research and Development, through its National Defense Research Committee, and to plan, present and supervise definite research projects for either war materials or armaments. The War Metallurgy Committee and its Advisory Committee, according to Dr. Jewett, is set up to function as the nerve center for all metallurgical research organizations and departments in this country. The heads of any business, university or research organization can be counted upon by this committee to make available the experience of their metallurgical scientists and engineers or their laboratory data. There are in excess of 10,000 such individuals in this country, and their combined experience represents well over 125,000 man-years.

One of the basic considerations in the operation of this committee is that of saving time, mistakes and money. When a problem is proposed, through either the WPB or the Office of Scientific Research and Development, immediate action can be obtained by telephone communication with the leading scientists on that particular subject; initial committee meetings are

often held within 24 hours and, if the request is urgent, within the same day a plan of procedure is laid down and submitted.

Every one in this country, and scientists and industrialists are no exception, is naturally anxious to contribute everything he can toward winning the war. New thoughts, new ideas, new short cuts, are constantly coming to the front. While it is not the place of the War Metallurgy Committee, according to Dr. Jewett, to be the repository for such suggestions and ideas, it recognizes as a very definite part of its wartime job the appraisal of such of these problems and possibilities as are referred to it by the WPB or the Office of Scientific Research and Development.

Another important function of the War Metallurgy Committee is to digest and make available to those properly interested through their participation in the war effort the results of both Canadian and English metallurgical research. Obviously both Canada and England have a great many of the same problems which confront us, and the interchange of information makes available to all the best thinking and practice of scientists and industrialists on both sides of the Atlantic.

Typical of the problems referred to this committee is one asking for improvement in welding processes. A subcommittee was immediately appointed, which collected all available known data from universities, engineering foundations and research departments of business organizations. The Project Section of the War Metallurgy Committee worked up the research indicated and research procedure; with the approval of the National Defense Research Committee and the Office of Scientific Research and Development, this research was placed with one of the university laboratories and compensated for on a cost basis from funds made available by OSRD.

Typical of requests for data and projects from the WPB is that of the effect of substitution of lead-silver for tin-lead soldering of tin cans used for food products. Since tin is the one important metal which is not found in the United States, even in low-grade ores, it is obviously important that the conservation of the present use of tin is urgent. Since a great proportion of the total consumption of tin is used in soldering, the substitution of lead-silver for tin-lead soldering is immediately dictated, but the problems involved in certain canning processes are such that definite research is needed before such substitution can be ordered.

This research project was prepared through the Project Section of the War Metallurgy Committee and will be administered through its research section, the work being done in one large university research laboratory, in cooperation with the National Canners Association.—*Chemical and Engineering News.*

SCIENTIFIC BOOKS

ASTRONOMY

Foundations of Astronomy. By W. M. SMART. 268 pp. 119 illustrations. London: Longmans, Green and Company. 1942.

THE preface of this excellent text announces that it "is intended for students taking a first-year course in Astronomy in the Universities and for all those interested in the subject who feel the need for a more solid foundation than the many descriptive books can provide." The book is definitely not descriptive in character; in the entire volume, there is not a single photograph or drawing of a celestial body. Only seven pages are devoted to the description of the sun, moon, planets, comets, minor planets and meteors, while nine pages are devoted to atmospherical refraction, fourteen to parallax and seventeen to aberration, precession and nutation. On the other hand, the volume is generously supplied with diagrams and sketches, clearly lettered, to help in the understanding of the text.

Although the book is essentially mathematical in character, the reader does not need a strong mathematical background to read it; nothing beyond a knowledge of elementary trigonometric functions is required. Only the cosine formula of spherical trigonometry is derived; the sine formula and several others are merely stated. The applications of the spherical trigonometric formulae are rather limited in number.

Five of the early chapters, "The Geometry of the Sphere," "The Celestial Sphere," "Right Ascension," "Mean Time" and "Determination of Position on the Earth," contain information needed as background by the student of navigation. Some of the terms used and the definitions given differ from standard American practise, enough to decrease considerably the value of the book to a person in the armed forces of the United States. For example, "true bearing" as defined by Smart is identical with "azimuth" as defined by the U. S. Navy; each is measured from the north point of the horizon to the east to 360°. "Azimuth" as defined by Smart is measured from the north point of the horizon in the northern hemisphere, from the south point of the horizon in the southern hemisphere; in either case, it is measured to the east or to the west to 180°. For purposes of computation, this definition is very convenient. He naturally pre-

sents the British measure of the nautical mile, 6,080 feet rather than the American, 6,080.27 feet.

In the discussion of time, the author carefully clears up one point on which there has been considerable confusion—the precise meanings of Greenwich Mean Time, Greenwich Civil Time and Universal Time, indicating the common usage of each in the United States and Great Britain.

Ten to twenty problems are provided at the end of each chapter to illustrate the principles therein; answers are given to all in the back of the book. The four chapters making up the last quarter of the book, "The Stars," Stellar Motions," "Clusters and Nebulae" and "Telescopes," also contain a minimum of description. The material throughout the book is up to date and clearly presented. The book fills a need for a modern text in elementary mathematical astronomy.

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SOCIETIES AND MEETINGS

THE AMERICAN PHYTOPATHOLOGICAL SOCIETY

The summer meeting of the American Phytopathological Society was held at Toledo, Ohio, on June 25 and 26. The theme of the discussions and reports was "The Role of the Plant Pathologist in the War Program." The activities of the War Emergency Committee, which was appointed at the Dallas meeting, were thoroughly discussed and suggestions for future activities were made. Considerable factual information was given in reports of available fungicides, substitute sprays and seed-treating materials and equipment priorities.

It was brought out that the depletion of the ranks of scientifically trained men constitutes a serious menace not only to present essential services to agriculture, but also jeopardizes the future because of the discontinuance of certain basic researches that are essential in furnishing a basis for intelligent action in plant disease control measures.

It was pointed out that losses from preventable diseases are still appalling. Epidemics often rage unchecked because proper control measures either are not taken at all—because they are not adequate, or because information regarding control measures had not been disseminated widely enough and at the proper time because of lack of sufficient trained personnel. One of the first and most important duties of plant pathology is prompt dissemination of information regarding the best available control measures. This responsibility can not be discharged properly under present conditions. A survey of the situation with respect to extension plant pathologists in the country indicates that very few states have an adequate extension service. Some states have no extension plant pathologist at all, and some of the most important agricultural states have a single extension plant pathologist, when two or three are needed. In only very few states can the situation with respect to extension work be considered satisfactory. Pathologists themselves are trying to do what they can by assembling and exchanging information, but the situation can not be alleviated properly until more men are made available for this very important phase of insuring the nation's supplies of essential materials from economic plants.

The following fields of research were cited as among those important to the nation's war effort: A better organized nation-wide plant disease survey service, fostered by the survey subcommittee, for effective direction of crop protection programs; work on new and improved fungicides and crop protection methods led by the fungicide subcommittee; development of disease-resistant crop varieties with coordinated, local trials under special subcommittees; research led by the seed certification and seed treatment committees on problems basic to certification or treatment of seed and planting stocks to reduce losses from seed- and plant-borne diseases; research on rotations, chemical treatment and cultural management of soils to reduce losses from soil-borne diseases; coordinated research on virus diseases of plants with entomologists helping on insect carriers; prompt investigation of newly discovered, potentially destructive plant diseases; research on diseases of new crops being grown to meet war-time shortages of oil, fibers, drugs, spices, etc.; more general study of soybean diseases; and work on effective home-made dusting, spraying and treating equipment where commercial equipment is unavailable.

It was brought out that the society's national and regional war emergency organization was well adapted for prompt exchange of research information. The necessity for adequate, coordinated plant disease survey work was repeatedly emphasized. Helpfulness of specialists in performing identifications for colleagues was commended. The *Plant Disease Reporter* was declared useful in facilitating such collaboration and for prompt dissemination of important new findings. Voluntary cooperation for adequate attack on many plant-disease problems was stressed. The tremendous national importance of plant disease eradication and control programs was said to demand their maintenance at highest efficiency during the emergency.

The War Emergency Committee consists of an executive committee, representatives of five geographical divisions, and members selected at large. Various subcommittees of the national committee have been appointed to take care of specific problems. The national committee is cooperating closely with the regional committees.

Executive Committee: J. G. Leach, University of West Virginia; Richard P. White, 636 Southern Building, Washington, D. C.; E. C. Stakman, *chairman,* University Farm, St. Paul, Minn.

The general objectives formulated by the committee are as follows:

(1) To provide for more adequate plant disease quarantines, foreign and domestic, to guard against introduction and distribution of new and destructive disease organisms.

(2) To intensify plant disease surveys to detect as soon as possible new disease introductions and to show where control efforts should be concentrated.

(3) To summarize and codify known control measures and make them available to extension men and growers in easily comprehensible form, and to encourage more adequate extension work in plant pathology.

(4) To attempt to get necessary priorities on chemicals and machinery used in controlling diseases.

(5) To concentrate effort on necessary experimentation and research designed to improve the effectiveness and economy of plant-disease control measures, by cultural practices, chemical treatments and resistant varieties.

(6) To summarize information regarding preservation of food and other products in storage and transit, make it available and provide for necessary studies to meet new situations.

(7) To scrutinize present basic and long-time research projects with a view to procuring support for those that are designed to yield facts and principles on which important procedures are based and those that could not be interrupted without serious loss of materials, accumulated results and experience.

(8) To maintain adequate personnel.

SPECIAL ARTICLES

THE EFFECTS OF JEJUNAL TRANSPLANTS ON GASTRIC ACIDITY[1,2]

ALTHOUGH a number of investigators have transplanted segments of jejunum into the wall of the stomach of animals for the purpose of observing the fate of such grafts, we are not aware of any published studies of the effects of such a procedure on gastric secretion. We wish therefore to report some observations on the free and combined acidity of the gastric secretion and the pH of various parts of the mucosa of the stomach before and after implantation of a pedicle graft of the jejunal wall.

Method: Mongrel dogs of both sexes were used for the experiments, which consisted in the resection under nembutal anesthesia of an area of the anterior wall of the stomach about 4 × 6 cm in size, midway between the cardia and pylorus, and the implantation into the resulting defect of a pedicle graft of upper jejunum with its circulation intact. This was obtained by isolating a segment 6 cm in length which was then opened along its anti-mesenteric border and fastened in place by means of interrupted sutures of silk. The continuity of the jejunum was restored by end-to-end suture.

The gastric secretion of each animal had been examined under nembutal anesthesia after 24 hours' fast at least once before beginning the experiments. At the time of operation direct measurements of the pH of the surface of the mucosa at seven definite areas in the stomach were made by inserting electrodes of the Beckman pH Meter through the defect in the anterior wall just prior to the implantation of the jejunal graft.

Subsequent gastric analyses were carried out in a similar fashion and pH determinations were made from 45 minutes to four months after the implantations, inserting the instrument through a gastrotomy. In two instances the transplant was then resected and further observations carried out.

Control animals were subjected to operations of similar length, as well as to resection of an area of the anterior wall of the stomach, after which the defect was closed without transplant.

The effects of this procedure on gastric secretion are most interesting, a striking feature being a reversal of the normal response to histamine in four of the five

TABLE I

pH OF GASTRIC MUCOSA BEFORE AND AFTER JEJUNAL TRANSPLANT
AVERAGE FIGURES FROM FIVE ANIMALS

	Before transplant			After transplant		
	Fasting	10 min. after histamine	20 min. after histamine	Fasting	10 min. after histamine	20 min. after histamine
Pylorus	4.6	2.3	2.3	5.2	5.4	6.0
Anterior antrum	5.0	3.7	2.7	5.7	6.1	6.1
Posterior antrum	4.3	3.2	2.7	5.7	6.5	5.9
Lesser curvature	4.8	1.9	1.4	5.2	7.0	5.9
Greater curvature	5.1	2.8	1.4	4.2	6.3	5.8
Fundus	5.2	3.5	1.5	3.6	6.3	5.8
Cardia	4.4	2.0	1.6	3.0	4.0	5.0
Composite averages	4.8	2.6	1.9	4.9	5.9	6.0

[1] From the Department of Surgery of the New York Hospital and Cornell University Medical College, New York.

[2] This study was carried out under a grant from the John and Mary R. Markle Foundation.

animals and a marked reduction in the fifth as demonstrated in the pH of the gastric mucosa of seven different regions of the stomach. These values appear in Table I, reference to which indicates that while in the average figures for five animals the fasting pH shows little change, the level after histamine is considerably elevated following the implantation of the jejunal segment.

The effect on the gastric analysis is also consistent and definite. Here the average fasting free and combined acidities are diminished somewhat after the jejunal transplantation has been performed and a further decrease occurs following histamine (Table II). Particularly noteworthy is the fact that the com-

TABLE II

GASTRIC ANALYSES BEFORE AND AFTER JEJUNAL TRANSPLANTS

	Before transplant			After transplant		
	Fasting	10 min. after histamine	20 min. after histamine	Fasting	10 min. after histamine	20 min. after histamine
Dog No. 1839						
Free	60	92	70	24	12	5
Combined ...	38	44	65	26	36	30
Total	98	136	135	50	48	35
Dog No. 1841						
Free	60	78	90	40	20	10
Combined ...	56	60	44	36	22	20
Total	116	138	134	76	42	30
Dog No. 1842						
Free	50	70	87	44	30	8
Combined ...	45	60	58	40	36	32
Total	95	130	145	84	66	40
Dog No. 1887						
Free	40	48	60	36	36	22
Combined ...	35	38	34	30	20	12
Total	75	86	94	66	56	34
Dog No. 1888						
Free	42	50	63	50	42	30
Combined ...	50	46	40	30	28	20
Total	92	96	103	80	70	50
Averages						
Free	50	68	74	39	30	15
Combined ...	45	50	48	32	28	23
Total	95	118	122	71	58	38

bined acidity is lower in each instance following operation, indicating that the reduction in free acidity is not to be explained on the basis of neutralization of the gastric juice by the alkaline secretion of the jejunal mucosa.

These changes have been shown to occur within 45 minutes of the transplantation and in the completely studied animals to persist for at least four months.

In two animals when the effects of the transplant were established, it was then resected and further pH measurements carried out. These indicated that within one hour one animal, number 1723, showed the normal reaction to histamine, although the fasting pH remained slightly higher than before the graft was implanted. In the other, number 1839, the pH of the mucosa and its reaction to histamine corresponded to the normal findings in all respects.

Further studies of the effect of such transplants on other aspects of gastric secretion are in progress.

PAUL STEFKO
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THE EFFECTS OF ANTI-MICROBIAL SUBSTANCES OF BIOLOGICAL ORIGIN UPON BACTERIAL TOXINS[1]

DURING recent years, the anti-microbial properties of various substances produced by different bacteria and fungi have been studied extensively and some of them have been utilized as chemotherapeutic agents in the treatment of infections of animals and man. Among the more important of these substances are the following: Pyocyanase, isolated from *Pseudomonas aeruginosa* by Loeb; penicillin, obtained by Fleming from *Penicillium notatum;* tyrothricin (gramicidin and tyrocidin) isolated by Dubos and Hotchkiss from *Bacillus brevis;* and actinomycin A and B isolated by Waksman from *A. antibioticus*. Although the action of these substances upon growth and survival of many bacteria and fungi is now well known, only scant information is available in regard to possible effects upon bacterial toxins. It has been stated that pyocyanase inactivates diphtheria toxin.[2] Tyrothricin and actinomycin A inhibit fibrinolysis by *beta hemolytic streptococcus* and plasma coagulation by pathogenic staphylococcus.[3] However, it is not known as yet whether these substances act directly upon fibrinolysin and coagulase themselves. In the following communication, the results of experiments on the effects upon bacterial toxins of various anti-microbial substances of biological origin are presented.

Tyrothricin, actinomycin A, pyocyanase and dimethyl-benzylammonium chloride (Zephiran) were tested for possible antitoxic activity. The latter substance was included because it is a mixture of alkyl radicals from C_8H_{17} to $C_{18}H_{37}$ as contained in the corresponding fatty acids of cocoanut oil. Tetanus toxin was diluted either in buffer solution (pH 7.2) or in infusion broth and then mixed with appropriate amounts of the respective substances. The mixtures were injected subcutaneously into the leg of white mice (18 to 24 g) either immediately or following incubation of 37° C for various periods of time. The animals were observed daily for the development of

[1] The author wishes to express his appreciation to Dr. D. F. Robertson, associate medical director, Merck and Company, for tyrothricin and pyocyanase; to Dr. Edwin F. Voigt, Director, Human Biological Division, Lederle Laboratories, for tetanus and diphtheria toxin; and to Dr. Selman A. Waksman, State of New Jersey Agricultural Experiment Station, New Brunswick, for actinomycin A.

[2] R. Emmerich, O. Loew and A. Korschun, *Zentr. Bakt. Parasitenk.*, 31: 1–25, 1902; Okhubo, *Z. Immunitaesf.*, 5: 428, 1910.

[3] E. Neter, *Proc. Soc. Exp. Biol. Med.*, 49: 163–167, 1942.

local or generalized tetanus and death. A few experiments were carried out with diphtheria toxin; guinea-pigs weighing from 150 to 250 g were used in these studies.

The experiments revealed that tyrothricin (0.05 mg and less) has no immediate effect upon the toxicity of tetanus toxin. The mixture of tetanus toxin and tyrothricin causes tetanus just as tetanus toxin alone. However, tyrothricin has a marked effect upon tetanus toxin which has been diluted in physiological salt solution or in buffer solution and kept either at 37° C or 4° C for 24 hours or more. Such a diluted toxin loses rather rapidly in toxicity. Tyrothricin in amounts of 0.05 mg to 0.000005 mg partially or completely inhibits this loss of toxicity of tetanus toxin. In one particular experiment, for instance, diluted tetanus toxin, which had been incubated together with tyrothricin at 37° C, caused tetanus and death, whereas the tetanus toxin control had become completely devoid of toxicity. It is interesting to note that tyrothricin also inhibits the loss of toxicity of tetanus toxin which has been exposed to heat (55° C). In regard to the mode of action, it may be pointed out that tyrothricin is a mixture of two polypeptides, namely, gramicidin and tyrocidin, and that peptones likewise inhibit the loss of toxicity of diluted tetanus toxin.[4] No evidence was obtained that tyrothricin increases the toxicity of tetanus toxin *per se*. It does not prevent the neutralization of tetanus toxin by the homologous antitoxin. Tyrothricin also inhibits the loss of toxicity of diphtheria toxin which has been diluted in physiological salt solution or buffer solution and kept at 37° C or 4° C.

Actinomycin A, an orange-colored pigment with marked bacterio-static activities, has no effect upon the toxicity of either diphtheria or tetanus toxins: in amounts of 0.005 mg and less, it neither prevents the loss of toxicity of these toxins which have been diluted in physiological salt solution, nor does it inhibit or enhance their toxicity.

Pyocyanase exerts a definite effect upon tetanus toxin. A preparation of pyocyanase was obtained from Merck and Company through the kindness of Dr. D. F. Robertson. It is a brownish, black slave-like material, soluble in ether and alcohol, but mainly insoluble in water. Following incubation for 24 to 48 hours, this pyocyanase preparation in amounts of 1 mg inhibits the toxic and lethal effects of tetanus toxin. This effect takes place in the presence of broth. Injection of tetanus toxin immediately after the addition of pyocyanase resulted only in a slight delay of the appearance of signs of tetanus.

Zephiran, too, exerts a definite effect upon tetanus toxin. In dilution of 1:10,000, it completely prevents the toxic effects of tetanus toxin in mice, even when the toxin is injected immediately following the addition of this substance. It is important to note that the effects of zephiran upon tetanus toxin are somewhat inhibited in the presence of infusion broth and even more so in the presence of human serum.

The foregoing experiments revealed that certain substances of biological origin with marked anti-microbial properties, such as pyocyanase and zephiran, inhibit the *in vivo* effects of tetanus toxin. Whether or not they irreversibly inactivate the toxin and change its antigenic pattern, remains to be determined. Certain others, such as tyrothricin, inhibit the loss of toxicity of tetanus and diphtheria toxins which have been diluted in physiological salt or buffer solution. The effects upon other bacterial toxins need further investigation, and it remains to be seen whether the antitoxic properties of antimicrobial substances of biological origin can be utilized with efficacy and safety in the treatment of localized and generalized infections in which bacterial toxins play an important role.

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[4] K. Halter, *Zeitschr. Hyg. Infektionskr.*, 118: 245–262, 1936.

CAROTENOIDS OF TELIAL GALLS OF GYMNOSPORANGIUM JUNIPERI-VIRGINIANAE LK.[1]

THE rust fungus *Gymnosporangium juniperi-virginianae* Lk. infecting the common juniper (*Juniperus virginiana* L.) forms caulicolous galls, globoid or reniform in shape, varying in diameter from 5 to 30 mm or more. The aeciospores produced during the summer on the cultivated apple are transferred to the juniper and cause infection. The mycelium remains dormant until the following spring when the telial galls become visible. These galls grow throughout the summer, mature in the fall and give rise to the teliospores the next spring.[2]

The mature galls used in this work were gathered when the telia were 1 to 2 mm in diameter by 5 to 10 mm long. The galls ranged in size from 10 to 50 mm in diameter and were of a cedar-brown color, while the telia were of a deeper reddish brown.

The leaves of the juniper contained 50 per cent. water at the time of gathering the galls, while the galls contained 68 per cent. water. The color of the interior of the galls when opened was pale green near the rind, while the body was light yellow. On exposure to the air, however, this color deepened to

[1] Contribution No. 274 from the Department of Chemistry.

[2] F. L. Stevens, "The Fungi Which Cause Plant Disease." Macmillan, 1921.

orange-yellow. Microscopic examination of the crushed galls showed that they consisted largely of teliospores and mycelium with the color confined to the teliospores.

Entire galls weighing 10 to 15 g were diced, weighed and placed in Erlenmeyer flasks. One hundred ml of saturated alcoholic potash was added and the whole refluxed for one-half hour. The gall residue was separated by suction filtration and the residue mixed in a Waring blender for 2 minutes with 50 ml of alcohol. The mixture was again refluxed for 15 minutes and the alcoholic extracts combined.

Complete removal of all the carotenoids present was accomplished with three extractions, using small amounts of petroleum ether (b.p. 30–60°). The pigments were epiphasic against 90 per cent. methanol, indicating the absence of free or esterified xanthophylls.

The combined petroleum extracts were dried over anhydrous Na_2SO_4 and brought to a small volume by distillation *in vacuo*. They were then chromatographed by the Strain[3] technic, using as adsorbent a mixture of MgO and Hyflo Super Cel (1:1). Only two zones separated. The lower zone was subsequently shown by spectrum analysis to be β-carotene. The upper, more strongly adsorbed red-orange zone had absorption maxima in petroleum ether at 4600Å and 4900Å with a minimum at 4800Å. The latter pigment, by its behavior on the adsorbent and its absorption spectrum, appears to be identical with γ-carotene.

The total carotene concentration of the gall was 3.31 mg per 100 g, of which 36 per cent. was β-carotene and 64 per cent. the γ-isomer. By comparison, a similar chromatographic study of the leaves gave 4.03 mg per 100 g of total petroleum-phasic carotenoids distributed as follows: 7 per cent. α, 83 per cent. β and 10 per cent. γ-carotene. Small amounts of xanthophylls were present in the leaves, but these were not investigated.[4]

The remarkably high content of the γ-isomer in the gall is of particular interest. This isomer is quite rare in plants, constituting only 0.1 per cent. of the total carotene prepared from ordinary sources.[5] Small amounts have been found in apricots (*Prunus armeniaca*).[6] Mackinney[7] has reported the marsh dodder (*Cuscuta salina*) to be a relatively rich source. Emerson and Fox[8] found a remarkably high concentration of γ-carotene in the male gametangia of the aquatic Phycomycete *Allomyces*. The latter workers point out the probability that "carotenoids may play important biological roles in sexuality and the process involved in the metabolism of reproduction."

The gall described is the richest source of γ-carotene which has come to the attention of the authors.

SUMMARY

In an investigation of the pigments of the telial galls of the common rust fungus *Gymnosporangium juniperi-virginianae* Lk. β- and γ-carotenes were shown to be the only carotenoids present, with the γ-isomer predominating. The identification of γ-carotene was based on its more characteristic properties, behavior on an adsorbent, and its absorption spectra. Neither free nor esterified xanthophylls were present, and only traces of chlorophyll.

The leaves of the juniper, besides containing chlorophyll, showed the presence of α-, β- and γ-carotene.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

CHROMATOGRAPHIC ANALYSIS IN REVERSE

THE adsorption of substances from solution has generally been accomplished in one of two ways: by shaking the solution with the adsorbent and then filtering or by means of a chromatographic adsorption column. In the latter, the solution is allowed to percolate through a column packed with an adsorbent and the various adsorbable substances in the solution form bands in the adsorbent column, which can later be removed and eluted separately.

Because of the recognized value of chromatographic analysis, a modification of this technique found in this laboratory appears to have interesting possibilities as a research method. This modification consists in reversing the usual Zwett technique. Instead of passing the solution through the adsorbent column and then separating the bands by washing, the solution is placed in a tube and the adsorbent allowed to settle slowly through it, a small portion at a time. The powdered adsorbent falling through the solution sets up eddy currents which mix the solution sufficiently.

[3] H. Strain, *Jour. Biol. Chem.*, 105: 523, 1934; *ibid.*, 111: 85, 1935.

[4] M. Tswett has reported the presence of the xanthophyll, rhodoxanthin, in *Juniperus virginiana*. *Compt. rend.*, 152: 788, 1911.

[5] R. Kuhn and H. Brockmann, *Naturwiss.*, 21: 44, 1933; *Ber.*, 66: 407, 1933.

[6] H. Brockmann, *Z. physiol. Chem.*, 216: 45, 1933.

[7] G. Mackinney, *Jour. Biol. Chem.*, 112: 421, 1935.

[8] R. Emerson and D. L. Fox, *Proc. Royal Soc. London*, 128: 275, 1940.

Tubes of various sizes may be used. Best results have been obtained using tubes of 4 to 12 mm inside diameter and 100 cm long. The tube is mounted vertically. This is important, since otherwise the solid will tend to pile up unevenly on the bottom and will not settle uniformly through the solution. A small funnel is attached with a rubber tube to the top end and the bottom is closed with a cork. Placing a funnel at the top of the tube makes it easier to add the adsorbent to a small tube without spilling. It also allows the powder to be wetted by the solvent and to fall slowly through the narrow neck of the funnel in such a way that it does not enter the tube in lumps. Six or more inches of the tube (depending on the total length) are filled with pure solvent and the solution to be treated is carefully poured on top of it. The tube is filled completely, the liquid extending up into the small funnel to a depth of several centimeters. The powder is added in equal measured amounts of 0.2 to 1 gram. The accuracy of separation which is desired determines the size of the portions, and this in turn depends on the width of the tube, the quantity of substance to be adsorbed and the ease with which it is adsorbed.

In a solution containing three adsorbable substances, A, B and C, whose affinity for the adsorbent decreases in the same order, a portion of adsorbent settling through the solution will adsorb substance A first. The following portions will continue to adsorb A as long as any remains in solution. When A is removed further adsorbent will begin to adsorb B and finally C in succession. If such substances are colored, the column of the settled layers of adsorbent thus built up will be found to be colored by A on the bottom, then by B and finally by C, while the top layer will be entirely colorless if an excess of adsorbent has been added. It is interesting to observe by this method that more strongly adsorbed solutes are eluents for less strongly adsorbed substances. This is, of course, obvious by definition, but is clearly demonstrated in the apparatus described. When several portions of adsorbent have passed through the tube and have adsorbed all substance A from the upper part of the tube, some will still remain in the lower portion. The next portion of adsorbent will adsorb substance B in the upper part of the tube and, as it falls further, will lose the color due to B and assume the color due to A because the B has been eluted by the more strongly adsorbed A remaining in the lower part of the tube. When finally all the A is gone and B is only present in the lower parts of the tube, the process is repeated by C being adsorbed at the top and then being eluted by B as it falls into the lower end of the tube.

The relative adsorptive abilities of two different materials can easily be determined by adding first one and then the other. When colored materials are being adsorbed, the least effective adsorbent will be least colored and will also serve to mark the positions of adjacent portions of the more active adsorbent. This effect can be utilized by using a non-adsorbing white powder with colored substances and a colored non-adsorbent when colorless substances are being treated. The addition of a small amount of such inert material between portions of adsorbent in this way very clearly indicates their position in the column thus built up and is a help in correctly sectioning it at the end of the experiment.

After the last portion of adsorbent has settled, the solvent can be carefully poured off and the tube allowed to drain. Then the cork is removed and the whole core pushed out and sectioned into its components. It is better to add quite a little adsorbent above the last colored layer so that when the solvent is poured off, just a little of this unimportant material will slide down the tube with the solvent while the desired portion of the core is not disturbed.

Investigation of this matter has been an incidental result of other work, the more pressing nature of which has, as yet, precluded further development of its potentialities. However, it is thought that the method has wide possibilities as a research tool in the field of adsorption analysis and may prove to be applicable to cases not amenable to methods previously described. Consequently, this method is brought to the attention of other research workers with the hope that those having the knowledge of the pitfalls and advantages of adsorptive procedures will investigate and develop it further.

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BOOKS RECEIVED

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